

Supplementary Table 1: International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis and procedure codes for comorbidities

Disease	ICD-9-CM Code	Description
Cardiovascular diseases		
Hypertension and hypertensive diseases	401	Essential hypertension
	402	Hypertensive heart disease
	403	Hypertensive chronic kidney disease
	404	Hypertensive heart and chronic kidney disease
	405	Secondary hypertension
Coronary heart disease	410	Acute myocardial infarction
	411	Other acute and subacute forms of ischemic heart disease
	412	Old myocardial infarction
	413	Angina pectoris
	414	Other forms of chronic ischemic heart disease
Heart failure	428	Heart failure
Chronic liver disease		
Chronic liver disease, liver failure, liver cirrhosis and complications	570	Chronic liver disease and cirrhosis
Diabetes mellitus		
Diabetes mellitus	250	Diabetes mellitus
Cancer		
Malignant neoplasm	140-149	Malignant neoplasm of lip, oral cavity, and pharynx
	150-159	Malignant neoplasm of digestive organs and peritoneum
	160-165	Malignant neoplasm of respiratory and intrathoracic organ
	170-176	Malignant neoplasm of bone, connective tissue, skin, and breast
	179-189	Malignant neoplasm of genitourinary organs
	190-199	Malignant neoplasm of other and unspecified sites
	200-209	Malignant neoplasm of lymphatic and hematopoietic tissue
Cerebrovascular disease		
Cerebrovascular events	430	Subarachnoid haemorrhage
	431	Intracerebral haemorrhage
	432	Other and unspecified intracranial haemorrhage
	433	Occlusion and stenosis of precerebral arteries
	434	Occlusion of cerebral arteries
	435	Transient cerebral ischemia
	436	Acute, but ill-defined, cerebrovascular disease
	437	Other and ill-defined cerebrovascular disease
	438	Late effects of cerebrovascular disease
Chronic obstructive airway disease		
Chronic obstructive pulmonary disease and allied conditions	490-496	Chronic obstructive pulmonary disease and allied conditions
Kidney diseases		
Nephritis, nephrotic syndrome, and nephrosis	581	Nephrotic syndrome
	582	Chronic glomerulonephritis
	583	Nephritis and nephropathy not specified as acute or chronic
	585	Chronic kidney disease
	586	Renal failure, unspecified
	587	Renal sclerosis, unspecified
	588	Disorders resulting from impaired renal function
Others	403.1	Benign hypertensive renal disease
	403.9	Unspecified hypertensive renal disease

04.12404.1	Benign hypertensive heart and renal disease
3	Unspecified hypertensive heart and renal disease
404.1	Polycystic kidney, unspecified type
404.9	Polycystic kidney, autosomal dominant
753.12	Polycystic kidney, autosomal recessive
753.13	Gouty nephropathy
753.14	Postural proteinuria
274.1	Unspecified disorder of kidney and ureter
593.6	
593.9	

ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification.

Supplementary Table 2: Baseline clinical characteristics and in-hospital outcome of patients with and without type 2 diabetes admitted with COVID-19 in Hong Kong between January 2020 and February 2021

	Patients with diabetes		Patients without diabetes		
	Number (%) with available data		Number (%) with available data		p-value
Demographics					
Age, years	1220 (100.0)	65.3 (57.1, 73.1)	9839 (100.0)	44.6 (32.3, 58.6)	<0.001
Men, n (%)	1220 (100.0)	662 (54.3)	9839 (100.0)	4047 (47.0)	<0.001
Ex- or current smoker	1220 (100.0)	209 (17.1)	9839 (100.0)	868 (10.1)	0.001
Metabolic parameters					
Diabetes duration, years	1220 (100.0)	1.4 (0.3, 3.4)	-	-	-
BMI, kg/m ²	114 (9.3)	23.6 (21.5, 27.3)	598 (6.1)	23.5 (20.9, 26.5)	0.380
HbA1c, %	886 (72.6)	7.4 (6.6, 9.2)	1901 (19.3)	5.8 (5.4, 6.3)	<0.001
Comorbidities, n (%)					
Hypertension	1220 (100.0)	644 (52.8)	9839 (100.0)	815 (9.5)	<0.001
Coronary heart disease	1220 (100.0)	130 (10.7)	9839 (100.0)	148 (1.7)	<0.001
Heart failure	1220 (100.0)	44 (3.6)	9839 (100.0)	44 (0.5)	<0.001
Cerebrovascular disease	1220 (100.0)	111 (9.1)	9839 (100.0)	148 (1.7)	<0.001
Chronic kidney disease	1220 (100.0)	249 (20.4)	9839 (100.0)	235 (2.7)	<0.001

Chronic liver disease	1220 (100.0)	44 (3.6)	9839 (100.0)	44 (0.5)	<0.001
Chronic obstructive airway disease	1220 (100.0)	61 (5.0)	9839 (100.0)	235 (2.7)	<0.001
Cancer	1220 (100.0)	83 (6.8)	9839 (100.0)	180 (2.1)	<0.001
Baseline drug use, n (%)					
Metformin	1220 (100.0)	737 (60.4)	9839 (100.0)	0	<0.001
Sulphonylureas	1220 (100.0)	385 (31.6)	9839 (100.0)	0	<0.001
DPP-4 inhibitors	1220 (100.0)	199 (16.3)	9839 (100.0)	0	<0.001
Thiazolidinediones	1220 (100.0)	90 (7.4)	9839 (100.0)	0	<0.001
SGLT-2 inhibitors	1220 (100.0)	78 (6.4)	9839 (100.0)	0	<0.001
GLP1 receptor agonists	1220 (100.0)	13 (1.1)	9839 (100.0)	0	0.011
Insulin	1220 (100.0)	273 (22.4)	9839 (100.0)	0	<0.001
Statins	1220 (100.0)	709 (58.1)	9839 (100.0)	572 (6.6)	<0.001
Blood pressure lowering drugs	1220 (100.0)	691 (56.6)	9839 (100.0)	1108 (12.9)	<0.001
RAAS inhibitors	1220 (100.0)	590 (48.4)	9839 (100.0)	452 (5.2)	<0.001
In-hospital treatment, n (%)					
Oseltamivir	1220 (100.0)	16 (1.3)	9839 (100.0)	63 (0.7)	0.051
Ribavirin	1220 (100.0)	396 (32.5)	9839 (100.0)	1823 (21.2)	<0.001
Lopinavir-ritonavir	1220 (100.0)	335 (27.5)	9839 (100.0)	1542 (17.9)	<0.001

Interferon beta	1220 (100.0)	725 (59.4)	9839 (100.0)	2702 (31.3)	<0.001
Antibiotic therapy	1220 (100.0)	755 (61.9)	9839 (100.0)	2769 (32.1)	<0.001
Anti-fungal therapy	1220 (100.0)	124 (10.2)	9839 (100.0)	265 (3.1)	<0.001
Corticosteroid	1220 (100.0)	623 (51.1)	9839 (100.0)	1747 (20.3)	<0.001
Pulse methylprednisolone	1220 (100.0)	5 (0.4)	9839 (100.0)	7 (0.1)	0.011
Intravenous immune globulin	1220 (100.0)	6 (0.5)	9839 (100.0)	9 (0.1)	0.007
Clinical outcome, n (%)					
ICU admission	1220 (100.0)	187 (15.3)	9839 (100.0)	269 (3.1)	<0.001
Mechanical ventilation	1220 (100.0)	110 (9.0)	9839 (100.0)	142 (1.7)	<0.001
In-hospital death	1220 (100.0)	90 (7.4)	9839 (100.0)	105 (1.2)	<0.001
ICU admission, mechanical ventilation and/or in-hospital death	1220 (100.0)	235 (19.3)	9839 (100.0)	340 (3.9)	<0.001

Data are presented as mean ± standard deviation or median (interquartile range) for continuous variables, and number (percentage) for categorical variables

BMI, body mass index; DPP-4, dipeptidyl peptidase-4; GLP1, glucagon-like peptide 1; HDL, high density-lipoprotein; ICU, intensive care unit; LDL, low density-lipoprotein; RAAS, renin-angiotensin-aldosterone system; SGLT-2, sodium glucose co-transporter-2

Supplementary Table 3: Laboratory results on admission and in-hospital treatment of patients with type 2 diabetes according to baseline use or non-use of metformin, sulphonylureas, DPP-4 inhibitors and insulin

	Metformin			Sulphonylureas			DPP-4 inhibitors			Insulin		
	Users	Non-users	p-value									
Number	737	254		385	679		199	952		273	623	
Laboratory results on admission												
Random glucose, mmol/L	8.1 (6.4, 11.0)	7.1 (6.0, 9.0)	<0.001	8.7 (6.5, 12.1)	7.5 (6.1, 9.7)	<0.001	8.7 (6.6, 11.9)	8.0 (6.4, 11.2)	0.108	9.2 (6.6, 12.8)	7.6 (6.2, 9.5)	<0.001
Sodium, mmol/L	137.0 (134.0, 139.0)	138.0 (135.0, 140.0)	0.018	137.0 (134.0, 139.0)	138.0 (135.0, 140.0)	0.001	136.0 (134.0, 139.0)	137.0 (134.0, 139.0)	0.01	136.0 (133.0, 138.0)	138.0 (136.0, 140.0)	<0.001
Potassium, mmol/L	3.9 (3.6, 4.0)	3.8 (3.5, 4.2)	0.938	3.9 (3.6, 4.3)	3.8 (3.5, 4.2)	<0.001	4.0 (3.7, 4.4)	3.8 (3.5, 4.1)	<0.001	4.0 (3.6, 4.4)	3.8 (3.5, 4.1)	<0.001
Creatinine, µmol/L	77.7 (63.0, 98.0)	83.0 (66.7, 124.0)	<0.001	81.2 (66.0, 110.0)	75.0 (62.8, 95.0)	<0.001	90.0 (70.0, 138.0)	75.0 (62.4, 94.0)	<0.001	91.3 (71.0, 140.0)	72.0 (61.0, 88.1)	<0.001
Albumin, g/L	38.4 (35.0, 41.3)	37.5 (33.0, 41.0)	0.006	38.0 (34.1, 41.0)	38.7 (34.9, 41.7)	0.076	37.0 (33.3, 41.0)	38.7 (35.0, 41.7)	0.019	36.0 (32.0, 39.4)	39.7 (36.0, 42.1)	<0.001
Total bilirubin, µmol/L	7.9 (6.0, 10.2)	8.1 (6.0, 12.0)	0.164	7.8 (6.0, 10.0)	8.0 (5.8, 11.0)	0.580	7.5 (5.4, 10.4)	8.0 (6.0, 11.0)	0.116	8.0 (5.8, 10.6)	8.0 (6.0, 10.6)	0.604
ALP, U/L	67.3 (55.1, 82.0)	74.0 (60.0, 92.4)	<0.001	70.0 (57.0, 84.0)	69.0 (56.0, 84.0)	0.752	70.0 (57.0, 83.0)	69.1 (57.0, 84.8)	0.789	69.3 (55.0, 88.0)	70.0 (57.5, 83.5)	0.843

ALT, U/L	27.0 (18.0, 39.5)	25.1 (16.9, 37.0)	0.295	27.8 (20.0, 39.4)	26.1 (17.0, 41.0)	0.142	26.0 (17.8, 34.9)	27.0 (18.0, 41.7)	0.145	24.4 (17.0, 36.0)	28.6 (19.0, 42.8)	<0.001
LDH, U/L	213.0 (178.0, 277.0)	234.0 (192.0, 303.0)	0.002	214.0 (183.0, 281.0)	219.0 (180.0, 281.0)	0.720	216.0 (190.0, 277.0)	217.0 (181.0, 283.0)	0.505	246.0 (192.0, 362.0)	209.0 (175.0, 254.0)	<0.001
CRP, mg/dL	1.3 (0.4, 4.7)	1.2 (0.3, 5.0)	0.980	1.7 (0.4, 5.4)	1.1 (0.4, 3.9)	0.032	1.5 (0.4, 5.3)	1.3 (0.4, 4.6)	0.376	2.9 (0.5, 7.5)	0.8 (0.3, 2.6)	<0.001
ESR, mm/hour	38.6 (21.0, 65.2)	47.0 (22.5, 84.1)	0.060	43.0 (20.5, 68.0)	37.0 (21.0, 64.0)	0.844	45.6 (21.5, 72.5)	39.8 (21.0, 68.0)	0.622	46.0 (25.0, 80.0)	34.0 (18.5, 53.5)	0.002
Procalcitonin, ng/mL	0.1 (0.1, 0.3)	0.1 (0.1, 0.3)	0.039	0.1 (0.1, 0.3)	0.1 (0.1, 0.3)	0.299	0.1 (0.1, 0.3)	0.1 (0.1, 0.3)	0.308	0.1 (0.1, 0.3)	0.1 (0.1, 0.1)	<0.001
Haemoglobin, g/dL	13.0 (12.0, 14.0)	12.9 (11.6, 14.2)	0.225	12.9 (11.8, 13.9)	13.2 (12.1, 14.3)	0.008	12.9 (11.6, 13.9)	13.2 (12.1, 14.3)	0.003	12.9 (11.5, 14.0)	13.2 (12.1, 14.2)	0.002
White cell count, $\times 10^9/\text{L}$	5.7 (4.6, 7.2)	5.7 (4.4, 7.2)	0.611	5.8 (4.8, 7.4)	5.6 (4.4, 7.0)	0.002	6.1 (4.6, 7.4)	5.6 (4.5, 7.1)	0.031	6.1 (4.8, 8.0)	5.5 (4.4, 6.9)	<0.001
Lymphocyte count, $\times 10^9/\text{L}$	1.2 (0.9, 1.6)	1.1 (0.8, 1.5)	0.044	1.2 (0.9, 1.6)	1.2 (0.8, 1.5)	0.451	1.1 (0.8, 1.5)	1.2 (0.9, 1.6)	0.138	1.1 (0.8, 1.4)	1.2 (0.9, 1.7)	<0.001
Platelet count, $\times 10^9/\text{L}$	204.0 (160.0, 254.0)	188.0 (149.0, 234.0)	0.003	206.0 (161.0, 258.0)	197.0 (156.0, 243.0)	0.027	204.0 (159.0, 249.0)	198.0 (156.0, 250.0)	0.336	199.0 (151.0, 255.0)	207.0 (166.0, 260.0)	0.101
Prothrombin time, seconds	11.9 (11.3, 12.5)	12.1 (11.4, 12.9)	0.006	11.9 (11.4, 12.6)	11.9 (11.3, 12.5)	0.819	12.1 (11.5, 12.8)	11.9 (11.3, 12.5)	0.026	12.1 (11.5, 12.9)	11.8 (11.2, 12.3)	<0.001
In-hospital treatment, n (%)												

Oseltamivir	9 (1.22)	2 (0.79)	0.739	5.0 (1.3)	10.0 (1.5)	1	3.0 (1.5)	11.0 (1.2)	0.72	7.0 (2.6)	6.0 (1.0)	0.074
Ribavirin	236 (32.0)	84 (33.1)	0.818	125.0 (32.5)	221.0 (32.5)	1	75.0 (37.7)	290.0 (30.5)	0.056	103.0 (37.7)	185.0 (29.7)	0.022
Lopinavir-ritonavir	200 (27.1)	73 (28.7)	0.681	110.0 (28.6)	184.0 (27.1)	0.656	53.0 (26.6)	256.0 (26.9)	1	93.0 (34.1)	125.0 (20.1)	<0.001
Interferon beta	425 (57.7)	164 (64.6)	0.063	220.0 (57.1)	409.0 (60.2)	0.357	122.0 (61.3)	556.0 (58.4)	0.498	187.0 (68.5)	309.0 (49.6)	<0.001
Antibiotic therapy	444 (60.2)	176 (69.3)	0.013	246.0 (63.9)	405.0 (59.6)	0.193	125.0 (62.8)	582.0 (61.1)	0.717	210.0 (76.9)	273.0 (43.8)	<0.001
Anti-fungal therapy	80 (10.9)	26 (10.2)	0.875	52.0 (13.5)	58.0 (8.5)	0.014	32.0 (16.1)	81.0 (8.5)	0.002	47.0 (17.2)	40.0 (6.4)	<0.001
Corticosteroid	367 (49.8)	142 (55.9)	0.108	201.0 (52.2)	330.0 (48.6)	0.286	108.0 (54.3)	475.0 (49.9)	0.296	168.0 (61.5)	203.0 (32.6)	<0.001
Pulse methylprednisolone	2 (0.27)	1 (0.39)	1	1.0 (0.3)	4.0 (0.6)	0.659	0.0 (0.0)	4.0 (0.4)	1	1.0 (0.4)	1.0 (0.2)	0.517
IVIG	2 (0.27)	2 (0.79)	0.272	2.0 (0.5)	2.0 (0.3)	0.623	0.0 (0.0)	5.0 (0.5)	0.594	2.0 (0.7)	0.0 (0.0)	0.093

Data are presented as median (interquartile range) for continuous variables and number (percentage) for categorical variables

ALP, alkaline phosphatase; ALT, alanine transaminase; CRP, C-reactive protein; DPP-4, dipeptidyl peptidase-4; ESR, erythrocyte sedimentation rate; IVIG, intravenous immune globulin; LDH, lactate dehydrogenase

Supplementary Table 4: Incidence rate, per 1,000 person-year, of clinical outcome from COVID-19 according to baseline use or non-use of metformin, sulphonylureas, DPP-4 inhibitors and insulin

	<u>Metformin</u>			<u>Sulfonylureas</u>			<u>DPP4-inhibitors</u>			<u>Insulin</u>		
	<u>Users</u>	<u>Non-users</u>	<u>p-value</u>	<u>Users</u>	<u>Non-users</u>	<u>p-value</u>	<u>Users</u>	<u>Non-users</u>	<u>p-value</u>	<u>Users</u>	<u>Non-users</u>	<u>p-value</u>
<u>ICU admission</u>	<u>4176.3</u>	<u>4063.2</u>	<u>0.879</u>	<u>6185.6</u>	<u>3042.6</u>	<u><0.001</u>	<u>4146.0</u>	<u>3958.9</u>	<u>0.814</u>	<u>7525.9</u>	<u>783.6</u>	<u><0.001</u>
<u>Mechanical ventilation</u>	<u>2101.5</u>	<u>1885.2</u>	<u>0.648</u>	<u>2894.0</u>	<u>1437.5</u>	<u>0.001</u>	<u>2287.6</u>	<u>1839.8</u>	<u>0.366</u>	<u>3519.7</u>	<u>179.8</u>	<u><0.001</u>
<u>In-hospital death</u>	<u>1258.8</u>	<u>2946.5</u>	<u><0.001</u>	<u>1673.1</u>	<u>1454.3</u>	<u>0.530</u>	<u>1561.2</u>	<u>1521.9</u>	<u>0.923</u>	<u>1734.8</u>	<u>977.2</u>	<u>0.036</u>
<u>ICU admission, mechanical ventilation and/or in-hospital death</u>	<u>4914.1</u>	<u>6633.4</u>	<u>0.043</u>	<u>7134.4</u>	<u>4202.9</u>	<u><0.001</u>	<u>5186.2</u>	<u>5100.3</u>	<u>0.924</u>	<u>8728.4</u>	<u>1615.4</u>	<u><0.001</u>

DPP-4, dipeptidyl peptidase-4; ICU, intensive care unit

Supplementary Table 5: Multivariate Cox regression with propensity score weighting for the association between baseline use of glucose-lowering drugs and clinical outcome

	Metformin		Sulphonylureas		DPP-4 inhibitors		Insulin	
	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
ICU admission, n (%)	0.51 (0.30, 0.86)	0.012	1.42 (0.90, 2.25)	0.131	0.46 (0.28, 0.76)	0.002	9.79 (4.26, 22.50)	<0.001
Mechanical ventilation, n (%)	0.29 (0.12, 0.72)	0.008	1.30 (0.70, 2.44)	0.405	0.42 (0.18, 0.98)	0.044	21.21 (4.40, 102.31)	<0.001
In-hospital death, n (%)	0.45 (0.23, 0.89)	0.022	2.87 (1.40, 5.88)	0.004	0.78 (0.38, 1.59)	0.487	2.86 (0.81, 10.13)	0.103
ICU admission, mechanical ventilation and/or in-hospital death, n (%)	0.53 (0.35, 0.81)	0.003	1.55 (1.02, 2.34)	0.04	0.48 (0.30, 0.76)	0.002	5.90 (3.41, 10.20)	<0.001

Adjusted for age, sex, smoking, diabetes duration, HbA1c level, comorbidities (hypertension, coronary heart disease, heart failure, cerebrovascular disease, chronic kidney disease, chronic liver disease, chronic obstructive airway disease, cancer), baseline use of other glucose-lowering drugs, statins and RAAS inhibitors, in-hospital use of other glucose-lowering drugs, and propensity score

CI, confidence interval; DPP-4, dipeptidyl peptidase-4; HR, hazard ratio; ICU, intensive care unit; RAAS, renin-angiotensin-aldosterone system

Supplementary Table 6: Multivariate Cox regression for the association between baseline use of glucose-lowering drugs and clinical outcome after excluding patients who were identified as having diabetes based on a single fasting plasma glucose (n=25)

	Metformin		Sulfonylureas		DPP4-inhibitors		Insulin	
	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
ICU admission	0.58 (0.35, 0.97)	0.039	1.48 (0.97, 2.25)	0.067	0.48 (0.29, 0.79)	0.004	12.49 (5.85, 26.68)	<0.001
Mechanical ventilation	0.49 (0.25, 0.97)	0.039	1.36 (0.77, 2.39)	0.286	0.62 (0.32, 1.20)	0.153	34.23 (4.40, 266.34)	<0.001
In-hospital death	0.47 (0.25, 0.90)	0.023	2.36 (1.21, 4.58)	0.011	0.70 (0.35, 1.39)	0.303	3.28 (1.21, 8.91)	0.020
ICU admission, mechanical ventilation and/or in-hospital death	0.53 (0.35, 0.82)	0.004	1.56 (1.07, 2.28)	0.020	0.47 (0.30, 0.74)	<0.001	6.44 (3.71, 11.20)	<0.001

Adjusted for age, sex, smoking, diabetes duration, HbA1c level, comorbidities (hypertension, coronary heart disease, heart failure, cerebrovascular disease, chronic kidney disease, chronic liver disease, chronic obstructive airway disease, cancer), baseline use of other glucose-lowering drugs, statins and RAAS inhibitors, and in-hospital use of other glucose-lowering drugs

CI, confidence interval; DPP-4, dipeptidyl peptidase-4; HR, hazard ratio; ICU, intensive care unit; RAAS, renin-angiotensin-aldosterone system